

Co-encapsulation of anti-BMP2 monoclonal antibody and mesenchymal stem cells in alginate microspheres for bone tissue engineering.

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Public Summary:

This study describes a technique for leveraging a system of mesenchymal stem cell-mediated, mAb-assisted bone regeneration. Here we describe a bone regeneration strategy based on in vitro and in vivo experiments which demonstrate the capacity of hBMMSCs (human bone marrow-multipotent stromal cells) to respond to the inductive signals provided by an anti-BMP2 mAb. We utilized the ability of anti-BMP2 mAb to trap and tether endogenous BMP2 (Bone morphogenetic protein 2) ligands for the directed osteodifferentiation of hBMMSCs using an RGD-alginate microencapsulation system. The advantages of this system include its simplicity and ease with which it can be modified to encapsulate hBMMSCs in an injectable and biodegradable alginate hydrogel, yielding a 3-dimensional, cell delivery scaffold for bone tissue engineering.

Scientific Abstract:

Recently, it has been shown that tethered anti-BMP2 monoclonal antibodies (mAbs) can trap BMP ligands and thus provide BMP inductive signals for osteo-differentiation of progenitor cells. The objectives of this study were to: (1) develop a co-delivery system based on murine anti-BMP2 mAb-loaded alginate microspheres encapsulating human bone marrow mesenchymal stem cells (hBMMSCs); and (2) investigate osteogenic differentiation of encapsulated stem cells in alginate microspheres in vitro and in vivo. Alginate microspheres of 1 +/- 0.1 mm diameter were fabricated with 2 x 10⁶ hBMMSCs per mL of alginate. Critical-size calvarial defects (5 mm diameter) were created in immune-compromised mice and alginate microspheres preloaded with anti-BMP mAb encapsulating hBMMSCs were transplanted into defect sites. Alginate microspheres pre-loaded with isotype-matched non-specific antibody were used as the negative control. After 8 weeks, micro CT and histologic analyses were used to analyze bone formation. In vitro analysis demonstrated that anti-BMP2 mAbs tethered BMP2 ligands that can activate the BMP receptors on hBMMSCs. The co-delivery system described herein, significantly enhanced hBMMSC-mediated osteogenesis, as confirmed by the presence of BMP signal pathway-activated osteoblast determinants Runx2 and ALP. Our results highlight the importance of engineering the microenvironment for stem cells, and particularly the value of presenting inductive signals for osteo-differentiation of hBMMSCs by tethering BMP ligands using mAbs. This strategy of engineering the microenvironment with captured BMP signals is a promising modality for repair and regeneration of craniofacial, axial and appendicular bone defects.

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